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The Bristol Medico-Chirurgical Journal

"Scire est nescire, nisi id me
Scire alius sciret."

AUTUMN, 1926.

THE RELATION OF THE AUTONOMIC NERVOUS SYSTEM TO CLINICAL MEDICINE.

Presidential Address, delivered on June 30th, 1926, to the Bath and Bristol Branch of the British Medical Association.

BY

J. R. CHARLES, M.A., M.D. (Cantab.), F.R.C.P.,
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THE autonomic nervous system plays such a paramount part in the manifestations of disease processes in the body, and the recognition of this is so important, that I have ventured to choose this subject for my address. The problems which it embraces are, however, so vast, and in many cases so little understood, that it will be only possible to touch the fringe of the subject; especially is this so when we realise what the autonomic nervous system does.

It influences those functions of the body without which the life of man cannot exist. It controls the metabolism of the body. It directs the action of all glands, whether these have an external or internal secretion. The action of the heart, vascular system,

and musculature of all the internal viscera are under its sway. Directly, or indirectly, it affects the mind. It is powerfully influenced by the mind. The mind, acting through it, influences the metabolism of the body. Through it the individuality of man is largely expressed. Through it we are born, and through it may die.

It is the primitive nervous system, much older in evolutionary development than the rest of the nervous system, to which so much attention has been given. We know much about the degenerations of the skeletal nervous system. What do we know about neuritis and localised degenerations of the peripheral parts of the autonomic nervous system ? Yet we have no reason for supposing that such lesions may not occur just as they do in the somatic nervous system.

Again, how much there is to be studied in the reflexes of the autonomic nervous system. These, or actions similar thereto, are very numerous, and probably as time goes on their clinical application will be more and more utilised. Concentration of thought on the working of these systems tends to make one realise how disease processes affect the body as a whole, and so directs our attention more and more to the patient who is suffering from the disease, rather than the disease merely considered as an entity in itself.

The autonomic nervous system is divided into three main groups : the cranial (mainly vagal), the thoracico-lumbar, and the sacral.

The vagal is anabolic, protective, and a builder of reserve.

The thoracico-lumbar, or sympathetic, is katabolic and largely useful in self-protection, for through its action primitive man could defend himself by fight

or flight, since it directly or indirectly increases skeletal muscular force, increases the heart rate, dilates the bronchi, allows more blood to go to the muscles, contracts the vessels of the skin, promotes perspiration, and restrains the activity of the gastro-intestinal functions. At the same time, it liberates more food in the form of sugar for the energy of the muscles. It therefore acts as a preserver of the individual.

Phylogenetically the vagal system is the older, the sympathetic system developing later, a point which has a bearing on the innervation of the sweat glands.

The sacral overflow is largely concerned in the continuance of the race, and is therefore the preserver of the race. In almost every form of disease the symptoms are largely of vegetative nervous origin. Through this system disease manifests itself.

The parasympathetic and sympathetic divisions are almost entirely antagonistic, and it is not surprising that with over-action or under-action of either part in disease we meet with the most diverse combination of symptoms.

Of the anatomy of the system we know much, but how little of the pathology or morbid anatomy. How often at autopsies is any attention whatever devoted to it ? Here lies a great future, the unravelling of a vast and difficult problem. We realise how little we know, and we grope in the dark, feeling that if only we knew how to control, to stimulate, or inhibit at will the different parts of the diverse sections of this mighty system then, as physicians, we could do what we now only dream of. In whichever direction we turn in disease we see the system profoundly affected, and we realise how remote or how widely spread the resultant manifestations of primarily localised disease may be.

There are many observers who consider that states of over-balance of the vagal or sympathetic systems exist among otherwise normal people. To these states the terms Vagotonia and Sympatheticotonia are applied.

Atropin paralyses the terminations of the parasympathetic, pilocarpin stimulates the parasympathetic. Eppinger and Hess found a group of people who were relatively insensitive to the effects of atropin, while unduly sensitive to pilocarpin. These they classified as cases of Vagotonia.

A difficulty, however, in accepting this view in its entirety is the action of pilocarpin on the sweat glands, which are supplied by the sympathetic nerves. The case for Vagotonia appears to have been overstated; but although this is so, there appear to be clinical conditions, at any rate, in which the vagal influence is over-active; *e.g.*, many cases of asthma, which are relieved by diminishing the irritability of the vagus by atropin, or by stimulating the antagonistic sympathetic by adrenalin, or by giving calcium, are almost certainly examples of a vagotonic syndrome. Probably anaphylaxis and serum disease are also parasympathetic syndromes, and are relieved by the same remedies.

It is perhaps noteworthy that conditions of Sympatheticotonia or Vagotonia can be observed in animals. This may involve differences even in the mode of death. For it is curious that a cat should die by a different mechanism from chloroform poisoning than does a dog from the same cause. A cat is sympatheticotonic, and probably dies by ventricular fibrillation due to sympathetic stimulation, while a dog, which is vagotonic, dies from vagal inhibition.

Observations such as these lead us on to consider

for a moment some of the manifestations of hyper-irritability of the sympathetic system in man.

Among the main manifestations we have a whole series of events which are essentially katabolic in nature, viz. prominence of eyeballs, dilatation of pupils, diminished secretions of lachrymal, salivary, nasal, gastro-intestinal tracts, the latter leading to hypochlorhydria and retarded digestion, diminished peristalsis of stomach and intestines, leading to one form of constipation, rapid pulse, and sometimes elevation of blood pressure, increase of blood sugar, contraction of uterus, increase of temperature (due to increased chemical changes) and vaso-constriction of cutaneous vessels, goose flesh, or increased sweating, and increased adrenal and thyroidal secretions. It is clear that these are outstanding features in many clinical conditions, and are also observable in very variable degree in people who are not technically ill, but who perhaps never seem quite fit. Such people appear to be much more susceptible to the effects of various viscerogenic reflexes than others.

These reflexes are extremely numerous. Reflexes occur between the sympathetic and the spinal nerves, not only in the segment of the cord which receives the afferent impulse from the viscus concerned, but also in segments far removed, the impulse passing by intercalated neurons in the cord. The same applies to the parasympathetic system. Thus we see that pressure in the nose may, by irritating the 5th nerve, produce asthma via the vagus.

Every important viscus is able to produce reflexes through afferent sympathetic and efferent spinal nerves in definite skeletal structures. If the viscus be acutely inflamed these reflexes produce alteration in sensation ; if chronically inflamed, trophic changes.

There are three main types of reflexes: viscero-motor, viscero-sensory, viscero-trophic.

The viscero-motor are represented by spasms in the skeletal muscles in the corresponding segments of the inflamed viscus. They are seen in the rigid abdomen, rigid thorax, in acute lung and abdominal diseases, spasm of the lumbar muscles in some renal complaints, and so on. It is characteristic of these that the muscle as a whole does not contract, but mainly that part which is supplied from the corresponding segment. The sterno-mastoids and trapezii may be similarly affected in acute cases of phthisis. If the condition persists it leads to a viscero-trophic effect, with wasting of the muscles.

The viscero-sensory reflexes are seen in the painful areas described by Head. Pain, however, from a diseased viscus may radiate over a much wider area than that supplied by the corresponding segmental skin area, as is seen in angina pectoris. With a relatively slight stimulus the pain may be precordial only, or with increasing stimuli, over the inner side of the left arm, or right down the inner side of the arm to finger-tips, or with even a greater stimulus down the right arm also. Moreover, similar reflex pains may be felt in later life, when there is then no longer any activity in the disease of the viscus. Such pains may occur if the patient is from any cause below par, or with changes in the weather, or when fatigued. The reasons for these pains frequently baffle us. The explanation of this probably is that when the pathway for pain has been opened by an adequate stimulus, the threshold of response to stimuli which ordinarily would produce no pain may be permanently lowered, so that pain results from a stimulus owing to a hyper-sensitiveness induced in the nerves concerned.

The viscero-trophic reflexes.—These are best seen in chronic visceral disease, particularly chronic pulmonary tuberculosis. Here we have the wasting of the muscles either in front or behind the upper part of the chest in apical phthisis, and the hilus "saucer of degeneration" described by Pottenger in the interscapular space in cases of hilus phthisis. In chronic disease of the kidneys, *e.g.* tuberculosis, there may be definite muscular wasting of the lumbar muscles. We see, therefore, that such a reflex may produce structural loss of tissue.

Perhaps one of the most striking features of clinical medicine is the variability of symptoms produced by the same disease in different people, a feature which adds so much difficulty to accurate diagnosis. This variability appears to be largely due to the difference in susceptibility of the "autonomic nervous system."

Examples are common enough. Take, for example, two cases of tuberculous peritonitis with the same pathological changes. One may have no symptoms to speak of, the other may suffer from such acute symptoms that the surgeon regards the case as an "acute abdomen," or the gastric ulcer which gives rise to no symptoms till it ruptures, or the gangrenous appendix which behaves in a similarly erratic manner, the latent pleurisy with effusion, or the terminal pneumonia unassociated with cough, expectoration, elevation of temperature, or increased respiratory rate.

It is true, of course, that other factors must be taken into consideration, such as the activity of the endocrine glands, and also the colloids of the cells of the body and their ionic content. Indeed, there seems to be some reason for believing that this latter condition may not only be responsible for a damping

off of symptoms, but even for a reversal of action, *i.e.* an effect from a given stimulation just the opposite from that which might have been expected.

Zondec found that stimulation of the sympathetic going to the heart throws out calcium into the perfusate, which if perfused through another heart gives the same result as sympathetic stimulation. Further, that if the vagus is stimulated potassium is thrown out into the perfusate, which if perfused through another heart gives the same result as if the vagus had been stimulated. Kolm and Pick showed that a hypersensitisation of one component of the autonomic nervous system such as might be produced by excessive calcium or potassium ionic content of cells may bring about a reversal of action, *i.e.* a parasympathetic effect when a sympathetic effect would have been expected, or vice versa.

Perhaps this is one of the reasons which may explain the abnormal idiosyncrasy which some patients exhibit towards certain drugs. I recently happened to be with a patient who was going to have a tooth removed under a general anæsthetic. She was given some atropin beforehand, and very soon afterwards she complained of cramp in all her limbs, which complaint continued until she was under the anæsthetic. On recovering from this she was in a condition closely resembling severe tetany, with such marked carpo-pedal spasms that it was with the greatest difficulty the fingers and feet could be straightened out. This condition continued for an hour or so. I was convinced that this state had been produced by atropin. No other drug had been given. How could such a clinical effect be produced ?

Tetany is a condition which is supposed to be due to parathyroid and calcium deficiency with consequent

hyper-irritability of certain parts of the nervous system leading to the well-known spastic symptoms. Possibly these may prove to be due to hyper-irritability of the sympathetic muscular nerves, the nerves of plastic tone. Similar spasms have been seen as the result of ergotism, and ergot stimulates the sympathetic. Atropin paralyses the parasympathetics, and there is no evidence of any parasympathetic innervation of the skeletal muscles. I can only, therefore, assume that in this case there was a reversal of action.

The episode to which I refer occurred about four months ago. The patient got well. A few days ago she had a most tempestuous voyage at sea with constant vomiting. She wrote to me saying that when she was so sick she lay on deck quite unable to help herself because "the cramps" had returned. This event supports, I think, the view that the condition was a true tetany.

T. P. Martin[1] has recently adduced the view that tetany is myogenous in character and not neurogenous. But there are other phenomena associated with tetany which appear inexplicable along the line of myogenic origin. I refer to changes in the skin, excessive sweating, changes in the hair and nails, and dysmenorrhœa. Moreover, the paroxysms may be excited by emotion. These are symptoms attributable to sympathetic over-action. Perhaps another explanation is that the atropin produced a sudden parathyroid deficiency. Both physical and psychical stimuli vary in their effects, some showing a preference for stimulation of the parasympathetic nerves, others of the sympathetic.

When we consider for a moment some of the symptoms of common diseases, we notice what a difference there is in the manifestations of toxæmias.

Compare two ordinary diseases, let us say typhoid and scarlet fever. Typhoid affects the alimentary canal, where the parasympathetic nerves are potent, and we meet with dry mouth, mental depression, sluggish eyes, and a pulse rate characteristically slow in proportion to the temperature—all suggestive of vagal predominance. Indeed, one of the diagnostic tests for typhoid is based on this. Marris's test consists of injecting 1/33rd gr. of atropin subcutaneously, under certain conditions. In a normal person the pulse rate would be raised markedly, say 30 beats per minute, owing to its antagonising action on the vagus. In typhoid, however, the trouble in the intestine appears to exert so marked a stimulation of the vagal endings in the intestine that the same dose of atropin fails to inhibit it in the same degree, and a pulse rise, therefore, of under 15 per minute, in a suspicious case, makes the inference that the disease is one of the typhoidal group very strong. This is therefore a test for abnormal vagus stimulation rather than a specific test for typhoid.

How frequently also is mental depression associated with disease of the intestine and liver. We have only to think of those people who suffer from membranous colitis. Diseases of the liver are notoriously depressing, the word " melancholia " itself being derived from the bile ; and circulating bile salts produce also the characteristic slowness of pulse.

Now in scarlet fever we see an entirely different clinical picture—bright eyes, red skin, increased respiration, and a pulse rapid in proportion to the temperature—a disease in which there appears to be over-stimulation of the sympathetic ; in fact, its manifestations are very similar in many ways to belladonna poisoning.

One wonders whether those toxæmias which are associated with a sympathetic over-stimulation may be those diseases in which nephritis is more prone to arise. The sympathetics are said to furnish both vaso-dilator, as well as the vaso-constrictor fibres to the kidney, and a definite vaso-dilatation would involve these organs being subjected to a greater amount of circulating toxin.

Bayliss found that stimulation of the posterior spinal roots either before or after passage through the ganglion produced dilatation of the vessels in the area supplied by the sensory nerve. These impulses he called "antidromic," or reversed impulses. Thus the same nerve fibre functions in opposite directions at the same time, sending sensory impulses upwards, and vaso-dilator impulses downwards. The eruption of herpes zoster is explained in this way, and it is interesting to remember that an association between herpes zoster and varicella has frequently been observed.

Heredity.

Many of the diseases which are transmissible by heredity are diseases largely of the autonomic nervous system, as, for instance, some forms of diabetes, gout, migraine, and asthma. To these perhaps may be added the myopathies. A dual innervation of the skeletal muscles has been fairly conclusively proved by Hunter, who drew the deduction that the skeletal muscles of vertebrates consist of two sets of muscle fibres, with different innervation and different functions. One of these nerve supplies is from the anterior horns and produces "contractile" tone, the other, being sympathetic in origin, producing "plastic" tone, *i.e.* a tone which maintains any posture when it has been assumed—a fixation tone.

Edwin Bramwell in the Bradshaw Lecture (Nov. 5th, 1925) brings forward very strong reasons in support of the view that the muscular dystrophies may be due to an affection of the sympathetic nervous system. The muscles primarily involved are those which are developed early in the fœtus, those which no longer fulfil the same important functions which they did in the earlier stages of evolution. Take, for example, the extrinsic muscles of the shoulder girdle, the serratus magnus, latissimus dorsi, rhomboids, and lower part of the pectoralis major. These, instead of forming a slinging system, as in a four-footed animal, now act mainly as fixing muscles for the arm, and also show atrophic changes early in the disease.

Atrophy and hypertrophy of the bones, a marbled condition of the skin, indicate that the disease is more than a localised muscular dystrophy. If, then, it is possible for the skeletal muscular sympathetic fibres to be susceptible to an early death, it is not surprising to find that an infant may be born with a preponderance of one part of the autonomic nervous system over another, or in other words that it may be vagotonic or sympatheticotonic.

Many of our emotions are closely associated with instinctive acts which have come down to us from remote ancestry, and are analogous to the anatomical structures of our bodies derived by evolutionary changes from lower forms of life and function. These changes act very largely through the autonomic nervous system, the result of many being well recognised, *e.g.* the lump in the throat felt in emotion, the dryness of the mouth through fear, the tongue cleaving to the roof of the mouth, or conversely the thought of something palatable making the mouth

water, the soundings of the bowels, the diarrhœa, polyuria of emotion, and so on.

Many of the normal physiological processes may be profoundly modified or disturbed by emotional disturbances. Thus digestion may be completely upset. Not only fear, but anger, has been shown experimentally in animals and in man, with gastric fistulæ, to inhibit gastric secretion, sometimes entirely. Indeed, these emotions may be so disturbing that taking appetising food even some hours later may fail to cause the normal flow of digestive juice; in other words, the effect of emotion may long outlast the exciting cause. It has been shown also that the flow of the pancreatic juice and of the bile are similarly influenced. During very great excitement gastric and intestinal peristalsis may entirely cease, a fact which has frequently been observed when examining animals with X-rays.

Hurst reports an interesting case of a nervous man whose gastric peristalsis was being examined by X-rays. The operator tapped the man with the screen under his chin, producing fear. All peristalsis immediately ceased, and moreover the stomach was seen to drop, so that he surmises, probably correctly, that the phrase "My heart dropped into my boots" should rather be, "My stomach dropped."

The psychical element must be taken into consideration when abdominal radiograms and gastric test meals are interpreted. Cannon, for example, refers to a woman with digestive disturbances who was sent for special examination by these methods. Her husband got drunk, and she spent a sleepless night before the examination. On examination the following morning no free HCl was found, no digestion of the test meal had taken place, but remains of the

supper of the previous evening remained. A repetition of the examination a day later, when the patient was calm and rested, showed normal gastric juice, normal digestion of test meal, and normal peristalsis.

Pain also will stop gastric peristalsis, or may produce nausea or vomiting, hence the expression "a sickening pain." The inhibition effects outlast the cause, a possible explanation of this being that the emotional cause stimulates the adrenals, liberating more adrenin into the veins, which substance, although it produces the same effects as sympathetic stimulation, acts directly on the viscera involved, and not through the nervous system.

By a variety of experimental methods Elliott and others have proved that artificial stimulation of the sympathetic nerves going to the adrenals causes a discharge of more adrenin into the circulation. The intestinal muscle of the rabbit is remarkably sensitive to the effects of adrenin, the normal rhythmical movements being inhibited by a dilution of 1 in 200 millions. Cannon has shown that blood taken from the inferior vena cava of an animal, where the veins from the supra-renal enter it, inhibits the rhythmical movements in the rabbit's intestine, if the animal has been subjected to excitement by etherisation, or fear, or pain, while this is not the case if the animal has not been subjected to these influences, but has merely been passive.

It has further been shown that the emotions produced by fear, rage, pain and also by mental effort produce an increase of sugar in the blood, and very frequently a temporary glycosuria. Four out of nine medical students after a difficult examination had sugar in the urine, while only one of the nine had it after an easier examination (Cannon). Twelve

cats (which are markedly sympatheticotonic) when artificially excited all showed marked glycosuria, though they had previously been free from this (Cannon).

One of the functions of adrenin is to liberate sugar from the liver, and sugar is the main source of muscular energy. Therefore perhaps we have one reason for the marked muscular weakness which is associated with Addison's disease, though perhaps it may be shown that other factors are operative, *e.g.* loss of plastic tone from loss of the sympathetic nerve force supplied to the small fibres of the skeletal muscles (Hunter). The low blood pressure would also have a deleterious effect in permitting fatigue metabolites to accumulate. Adrenin itself, moreover, lowers the fatigue threshold of neuro-muscular activity and causes forcible contractions.

Adrenin given in small doses increases the coagulability of the blood, and this may also be produced by splanchnic stimulation, which acts by increasing the amount of adrenin. Probably there is some co-operation between the adrenin and the liver, as this diminution of the coagulation time of the blood does not occur in the absence of the liver. Rage and pain also increase the coagulability of the blood, which is almost certainly due to adrenal discharge acting through splanchnic stimulation.

It is interesting to note that the optic thalamus is the centre representative of the protopathic aspect of peripheral sensibility, as well as the central base of emotive reactions, that Rivers regarded the emotive instincts as protopathic in character, and also that antidromic impulses pass along the protopathic nerves.

The emotional states which are manifested in the sympathetic division of the autonomic nervous system

are more intense than those manifested in the other divisions, because the sympathetic is the preserver of the individual. We see an example of this in bad spasmodic asthma. A patient who may be breathing with the greatest difficulty will get complete relief if he receive a severe stimulus of fear. He will therefore run with ease from his burning bedroom, the sympathetic response called into play by the emotion completely overcoming his previous vagotonia.

The Brain.

Some reference must be made to disorders of the brain and the autonomic nervous system. These disorders are seen both in organic and functional or psychical troubles.

There is almost always some evidence of disturbance of the sympathetic nervous system in hemiplegia, from whatever cause this arises. These phenomena may be increased blood pressure in the affected side, as compared with the other, increased elevation of temperature, and diminished sweating, passing frequently into exactly the opposite condition, viz. diminished temperature, lowered blood pressure, and increased sweating. The early hyperthermal syndrome is attributed to paresis of the sympathetic system and is associated with flaccid paresis, the second stage being hypothermal, analogous to the spastic stage of hemiplegia.

Passing on to psychical considerations, it seems quite possible that dreams, more particularly those which are distressing and associated with states of fear, like night terrors in children, working through the emotional centres, uncontrolled as these are during sleep by the higher reasoning faculties, may lead to definite functional changes in the autonomic system,

and perhaps play a part in the ætiology of many obscure conditions; for we have seen that the effect of an emotion outlasts its existence.

Eustace Smith described, in association with night terrors, a condition which he called "mucous disease," in which the patient is languid, irritable, sallow, constipated, with an excess of mucus in the motions, with abdominal discomfort, cyclic albuminuria and vaso-motor disturbances.

The emotions are, of course, phylogenetically much older than the reasoning faculties of mankind. Hence we should expect emotional responses to be more manifest in childhood before the reasoning faculties are developed. The fact that in childhood there is very marked instability of the autonomic system is seen in the liability in the early months of life to spastic conditions of the spincters of the gut, viz. hypertrophic stenosis of the pylorus, of the ileo-cæcal sphincter, and of the pelvi-rectal sphincter, leading to Hirschsprung's disease, whilst later in infancy there is a liability to an irregular form of peristalsis resulting in intussusception.

Even if we consider individuals in health, we meet an infinite number of variations, but certain types stand out. The impulsive, energetic, intense lady who speaks to us quickly and emphatically, though not perhaps very logically, with rapid movements and a frequent slight retraction of the upper eyelids, is she not a physiological example of an inherently over-active sympathetic nervous system? All out-put, katabolic, liable to nervous breakdowns? She may have a feeling of exaltation and well-being, but she is living dangerously, and exhaustion lies in wait, which may lead to disorder of the digestion, or such diseases as diabetes.

As we have seen, the autonomic nervous system is outside the action of the will. But even to this there are exceptions. A case has been recorded by Timme [2] in which a man could at will dilate his pupils, produce goose skin in any part of his body he desired, and raise the hair on his arms. This he did, not by direct voluntary effort, but by intensely imagining the appropriate stimuli which would call forth such reactions. For example, to produce goose skin he imagined his arm thrust into ice-cold water. So we see that imagination may produce effects the nature of which may readily be mistaken from the clinical aspect.

A somewhat interesting point here arises in connection with acting, *i.e.* whether a physical simulation of an emotion tends actually to produce that emotion. Do actors really feel their parts or not ? The question was put some years ago to the leading actors of the day, and the replies were in flat contradiction to one another. Much probably depends on the nervous make-up of the actor, some good actors not only being able to feel their part, but live in it for the time. If so, one would ask, Can these simulated emotions produce the same visceral effects as emotions produced in the usual ways ? Edmund Burke in a passage "On the Sublime and Beautiful" says : "I have often observed that on mimicking the looks and gestures of angry, or placid, or frightened, or daring men I have involuntarily found my mind turned to that passion whose appearance I endeavoured to imitate ; nay, I am convinced it is hard to avoid it, though one strives to separate the passion from its correspondent gestures."

William James gives the following explanation of the discrepancy in the replies of the actors : "The

visceral and organic part of the expression can be suppressed in some men, but not in others, and on this it must be that the chief part of the felt emotion depends. Those actors who feel the emotion are probably unable, those who are inwardly cold are probably able, to effect the dissociation in a complete way."

Furthermore, there is a disease in which people by continual concentration of their thoughts on their internal viscera bring into the realm of consciousness sensations of movements of these viscera, which normally do not pass the threshold of consciousness. It is possible that normally such impressions do reach the brain, and though unperceived as such, may colour the individuality, probably forming an integral part in the causation of feelings such as "well being," "melancholia," and so forth. Patients whom we call hypochondriacs can, however, give us accounts of sensations from the viscera with an intimate knowledge, of which the normal person knows nothing. They appear to have developed a new sense, which unfortunately increases their discomfort.

There appears to be very strong evidence to support the view that damage to, or irritation of, the different sections of the autonomic nervous system may lead to very definite structural changes. Consider, for instance, the following examples in connection with the vascular system. Lapinski showed that severance of the cervical sympathetic in rabbits led to changes in the arteries which consists of atrophy of the media and thickening of the intima, though in some cases the media was thickened.

In dogs it has been shown by experiments by Manouélian that if a nerve filament be removed which goes to a certain part of the abdominal aorta

atheromatous plaques are formed at that spot. Similarly he removed a nerve filament going to the part of the pulmonary artery in a dog. After 65 days a sclerosed patch was found at the part, the pathological changes being similar to those found in human beings in arterio-sclerosis.

Wingate Todd (1913) found arterio-sclerotic changes in a radial artery presumably due to nerve irritation from a cervical rib, while Stopford in 1918 found very marked similar changes in the distal arteries, following gunshot injuries to nerves much higher up in the limbs.

Some very interesting work has more recently been carried out by R. Cunliffe Shaw.[3] Very briefly these experiments, which were carried out in rabbits, consisted of the production of irritative lesions of the cardio-aortic nerves and subsequent investigation of the aorta. He first applied electrical stimulation externally from a 2-volt accumulator and induction coil along the vagal or sympathetic paths, the strength of the stimulus being just short of that which apparently produced pain. When the vagal path was irritated there was slowing of respiration and heart beat, while there was quickening of both these and prominence of the eyes when the sympathetic was irritated. The duration of the stimulus was ten to sixty minutes, with intervals of five or six days between the stimulations. Pathological changes occurred in every case, and included such lesions as dilatation of right ventricle, thickening of mitral valve, large and small nodular thickening of the aorta, and sclerosis of the cusps of the aortic valve.

The second method he used was to expose the nerves to the irritation of the air, and by the production of scar tissue around them. Twenty-two operations were performed on the vagal path, five on the

sympathetic and five on the depressor. Unfortunately, all these nerves may have been affected in each case owing to the amount of scar tissue produced, and therefore it was impossible to say which fibres were the cause of the production of the lesions. Irritation of the vagi produced endarteritis of the aorta, especially of the first part in ten out of thirteen rabbits. Irritation of the sympathetic produced similar results in four out of five rabbits. Irritation of the depressor again produced similar results in two out of five, but two died at the operation.

"The pathological changes are constant ones, and progress through a definite sequence, the earliest consisting of a proliferation of the intima, in which both endothelium and areolar and elastic tissues participate. This is followed by hyperplasia of the elastic fibres in the media and early signs of degeneration in the smooth muscle cells. Fat is deposited in the intima, and the deep layers of this zone undergo necrosis, with the formation in advanced cases of atheromatous abscesses, sloughing of the inner layer of the intima, and the formation of ulcers."

The Blood.

In many cases in which there is an over-action of the parasympathetic nervous system we find associated with it an eosinophilia. Asthma may be taken as a typical example. Why this should be I know of no answer. It is true that many of the causes of eosinophilia are associated with vagus irritation, *e.g.* worms in the intestine. But then again we meet with eosinophilia in such diseases as trichiniasis in muscles.

There is much to be learnt on the question, why different toxæmias should lead to different blood pictures, why in one complaint there should be

leucocytosis, in others lymphocytosis, in others eosinophilia. Is there any evidence of nervous control of leucocytic activity by the autonomic nervous system? Mueller[4] has made the following observations:—

Injection of non-specific albumin preparations, of minute amounts of salt solution, of distilled water, or even of air intradermally, produces an immediate leucopenia in the whole of the peripheral circulation, which lasts from five to thirty minutes, the cells migrating to the splanchnic area. Fifty to seventy-five million cells migrate from one area to another.

About 0·2 cc. of a solution of albumin is required. If given subcutaneously, intramuscularly, or intravenously the reaction does not occur. Expressed in percentage, the decrease is not influenced by pre-existing conditions of the blood, *e.g.* in a normal person the drop is from 8,000 to 5,000, in conditions associated with leucocytosis (*e.g.* pneumonia) from 25,000 to 16,000, in leukæmia say from 150,000 to 80,000. A similar decrease is seen in conditions associated with leucopenia, *e.g.* pernicious anæmia 5,000 to 1,600.

The substances injected are unable by themselves to produce organic changes in the body. By blocking the nerves which carry the vaso-dilator fibres in the splanchnic area it is no longer possible to produce these changes. Atropin and adrenalin, if given subcutaneously in any part of the body, make it impossible to produce this reaction of influence on the leucocyte count by intradermal injection.

Adrenalin, as we know, stimulates the sympathetic system. Atropin paralyses the parasympathetic. Pilocarpin, on the other hand, which stimulates the parasympathetic, does not change the influence of

the intradermal injections on the leucocytic reaction. In fact pilocarpin itself produces a drop, but a still further drop ensues when the intradermal injection is given.

The skin stimulation is supposed to be associated with a sudden change in the vascular system of the splanchnic area. If the nerves accompanying the large vessels going to a limb are severed, the intradermal injection in that limb no longer produces a general peripheral leucopenia. If, on the other hand, the intradermal injection is made into any other part of the body the diminution of leucocytes does occur in the general peripheral circulation, except in the extremity in which the nerves have been severed. These experiments show that the splanchnic area is not the only one involved. The part played in the extremity in which the nerves have been severed is not, therefore, merely a passive one. It was an active process which has been stopped by the severance of the nerves.

If a very diluted solution of adrenalin (1 in 100,000) is injected hypodermically a leucopenia is produced in the adjacent blood vessels, and curiously this only affects the polymorphonuclear leucocytes, the lymphocytes and other cells remaining as before.

The same author has made some most interesting observations on insulin shock in diabetic patients. Insulin shock shows itself by dizziness, weakness, trembling, profuse perspiration and collapse. As the blood sugar decreases so the leucocytes in the peripheral blood increase. In two cases which he observed the leucocytes reached 28,000 and 19,000. This increase from the normal occurred in fifteen minutes. In each case glucose was given (5 grammes in 100 cc. of water). In less than ten minutes the

leucocytes had fallen to 7,000. He attributes the shock to parasympathetic overbalance, and says that there is a simultaneous sympathetic overbalance in the splanchnic area. He suggests that all these observations tend to show that the periphery, as represented by the skin, and the splanchnic area, as represented by the liver, are controlled by one centre, and that the sugar centre in the medulla may act in connection with this. A mutual control of the skin and splanchnic area may lead to completely new conceptions. "Where parasympathetic stimuli predominate in the vascular system," he writes, "there the leucocytes will accumulate, while an overbalance of sympathetic stimuli produces a decrease of leucocytes in this region. Both processes originate in the autonomic nervous system, the migration of leucocytes being but a sequel."

We must not, therefore, dogmatically assume that a blood film taken in the usual way from the peripheral circulation represents the state of the blood throughout the whole of the body.

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[1] *Quarterly Journal Medicine*, 1925–26, vol. xix., p. 311.
[2] *Journal of Nervous and Mental Diseases*, 1914, vol. xli., p. 517.
[3] *Quarterly Journal Medicine*, 1925–26, vol. xix., p. 203.
[4] *Archives of Internat. Medicine*, 1926, vol. xxxvii., p. 268.

THE PATHOLOGY OF CERVICAL EROSION.[1]

BY

GEOFFREY HADFIELD, M.D., M.R.C.P. Lond.,
Pathologist to the Bristol General Hospital.

THE simple epithelium of the cervix uteri begins to differentiate about the third month of fœtal life into two types, that lining the cervical canal becoming columnar and, by invagination, forming a system of mucus-secreting glands, that covering the vaginal portion becoming squamous and laminated. At birth, the boundary between these two epithelia normally lies just within the lips of the external os, so that no glandular tissue is visible from the vagina. Occasionally, by faulty development, the columnar epithelium of the canal covers the vaginal portion of the external os over a circular area of varying size, producing the so-called congenital erosion of infants. This condition, purely developmental in origin, is a congenital, or, strictly speaking, a dysembryoplastic heterotopia and is usually corrected, the exposed ring of gland tissue being exfoliated by inward growth of the squamous tissue as far as the boundary-line. During this process and during the epithelial differentiation of the normally-developed cervix the two types of epithelium are in close association, and it is usually agreed that they replace each other with comparative ease and that degradation of columnar to squamous cells occurs readily.

The familiar acquired erosion of multiparous women,

[1] A Paper read at the Bath and Bristol Branch of the British Medical Association, May 26th, 1926.

although in all probability of different origin, is nevertheless due to heterotopia of cervical gland tissue. The epithelium of the external os disappears and proliferating gland tissue continuous with that lining the canal replaces its squamous lining. It is possible that in a few cases the condition is explained by inflammatory hyperplasia of congenitally heterotopic glandular tissue; some cases may be due to actual ectropion of the lining of the canal during labour, but it appears that the majority are due to the chronic endo-cervicitis of repeated pregnancies or of gonococcal infection, and that the squamous lining of the os is actually pierced by inflamed glandular tissue which presents at the external os as a reddened, roughened and irregularly shaped area—the simple glandular erosion (see Figs. 2 and 3). Several factors tend to endow the common glandular erosion with a considerable degree of chronicity and to alter its structure. In the first place, surface infection is common, so that increased vascularity and replacement fibrosis are present in inverse ratio. Next, the glandular tissue undergoes secondary changes, frequently becoming cystic (Fig. 3), and when of long standing the surface of the erosion often becomes covered by fine delicate papillæ (papillary erosion) due to projection as multiple polypi of the inflamed œdematous interstitial tissue lying between the gland mouths (Figs. 5 to 8). Finally, there is always a strong tendency for the squamous epithelium at the margin of the lesion to grow inwards and cover it, and for islands of surviving squamous cells isolated in it to grow over it. If this is successful, sheets of squamous cells grow into the ducts and tubules of the glands, which become exfoliated over large areas. In many cases this process of epidermisation is considerably delayed by the chronic irritation of surface

PLATE VI.

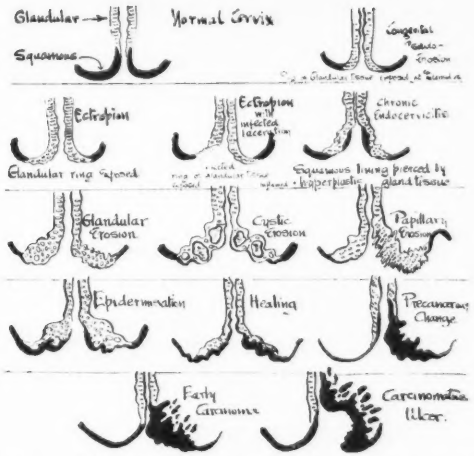


FIG. 1.—*Diagram illustrating varieties of erosion and changes leading to malignant disease.*

FIG. 2.—*Simple glandular erosion in early stage.*

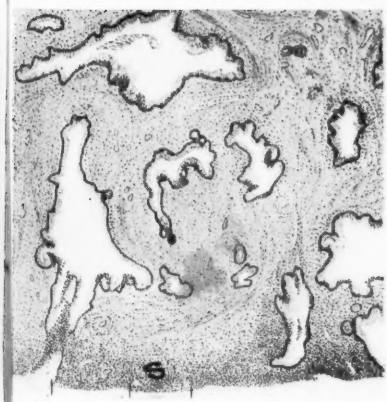


FIG. 3.—*Preceding under low power.*
S.—Infected surface.

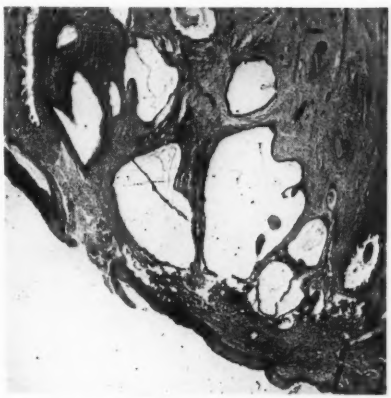


FIG. 4.—*Cystic erosion. Low power.*

PLATE VII.

PAPILLARY EROSION.

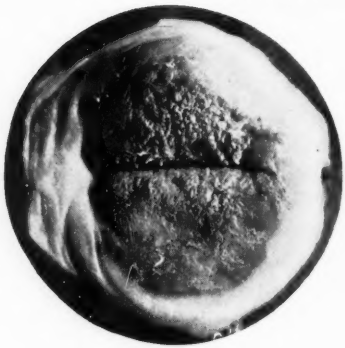


FIG. 5.—*Natural size.*

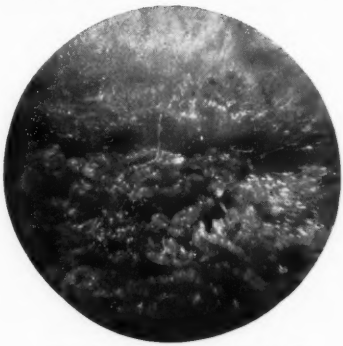


FIG. 6.—*Edge of lesion* (×8).

FIG. 7.
Surface at external os (×8).

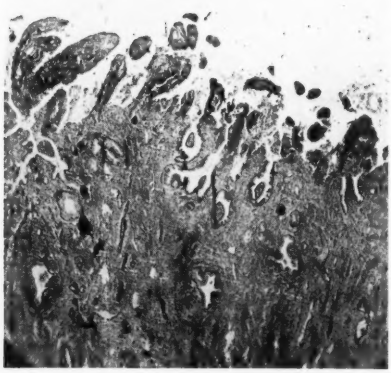


FIG. 8.
Section of preceding, low power.

and endocervical infection, whilst in some the repeatedly frustrated attempts at healing end in the production of foci of atypical and irregularly-laminated squamous-celled overgrowth, leading to the formation of islands of leukoplakia, to wart-like local overgrowth or to uniform coarse papilloma formation.

Along with these changes of gross structure there occur all those changes in the cells themselves which are styled pre-cancerous, including cellular and nuclear heteromorphism, increased mitoses and nuclear hyperchromatism. Such appearances are a commonplace in the routine examination of cervical tissue removed for intractable erosion, and are precisely the histological changes which so frequently precede malignant disease on every squamous-lined surface in the body. It cannot be too strongly urged, however, that such changes are not sufficient for a diagnosis of malignant disease until infiltration of deep tissue becomes manifest, and there is no doubt, as in the case of similar lesions of the tongue, that this dangerous-looking but non-infiltrating epithelial overgrowth may exist in an unhealed lesion for so long a time, that its malignant potentialities become insignificant, whilst in a few cases satisfactory healing may follow. In other words, although the malignant potentialities of these lesions are high, one cannot, with certainty, predict a malignant termination for them. Herein lies the immense importance of deciding how frequently intractable erosion is the forerunner of cervical cancer. It is not enough to find the two lesions clinically associated: they are both so common that a very large series of clinical records extending over many years would be necessary to gain reliable information. The problem is precisely similar to the determination of the frequency of malignant transformation of a chronic gastric ulcer,

except that in the case of erosion the histological criteria necessary for proof are considerably less liable to lead one into fallacy than in the case of ulcer-cancer of the stomach.

To establish the fact that an erosion has become cancerous we must find in the same cervix the typical glandular heterotopia of erosion in intimate relation with the infiltration of cancer, and satisfy ourselves that the erosion was the primary lesion. We must also find out how far the secondary changes produced by cancer in the glandular tissue of the cervix may copy those of erosion, and how far those produced by erosion may copy those of cancer.

I have for some time past examined all types of erosion coming to the laboratory as routine specimens ; and, employing these criteria, I find that when any case has shown clinical signs of malignant disease, it is usually difficult to demonstrate the typical lesion of erosion in intimate relation with the new growth, as the latter very rapidly overwhelms what is, after all, a superficial process. The specimens shown in Figs. 9 and 10 are, however, exceptions to this, erosion and cancer existing side by side. From the material I have seen the most conclusive evidence comes from cases in which a chronic and intractable erosion was excised, but in which clinical evidence of malignant disease was lacking. In such cases, if many sections are cut, it is not at all uncommon to find single and often microscopic foci where the widespread squamous overgrowth has assumed the characters of malignant disease.

The earliest case I have seen is that illustrated in Figs. 12 to 16, from which the minute dimensions of the focus can be judged by following it through increasing magnifications. It is in such material, in which cancer is not clinically obvious nor even suspected, that I have

PLATE VIII.

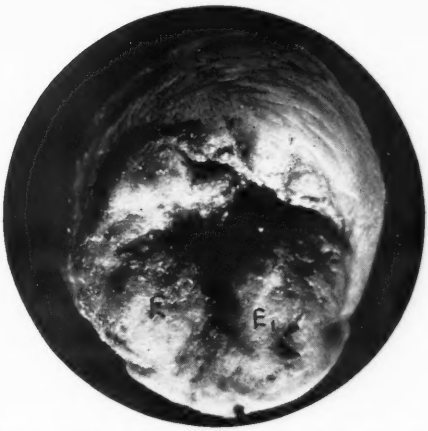


FIG. 9.—*Malignant transformation of erosion.*
Heaped-up malignant tissue replaces cervix except at E and E1, where appearances—confirmed by section—are those of erosion.

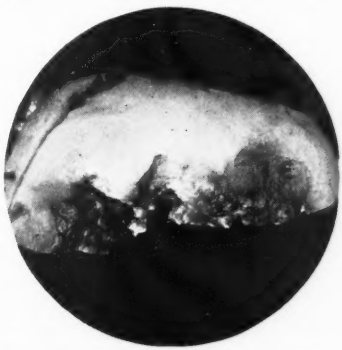


FIG. 10.—*Half a malignant cervix.*
Typical lesion of erosion remains over area E.

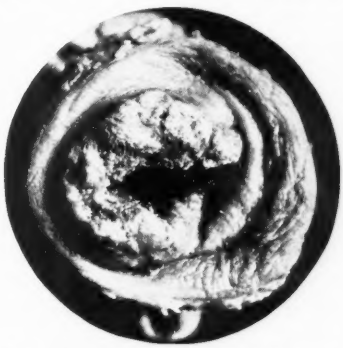


FIG. 11.—*Carcinomatous ulceration.*
No trace of erosion microscopically. History suggests previous erosion.

PLATE IX.

MICROSCOPIC FOCUS OF EARLY CANCER IN A TYPICAL EROSION.

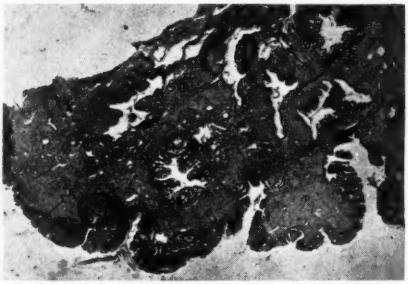


FIG. 12.—*Section of whole lesion. Malignant focus in circle.*

FIG. 13.—*Shows intimate relation of cancer and erosion* (G).

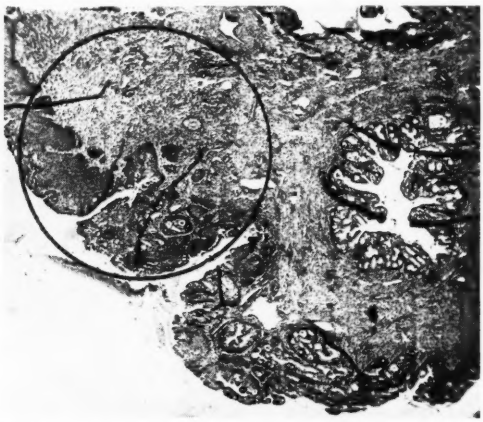
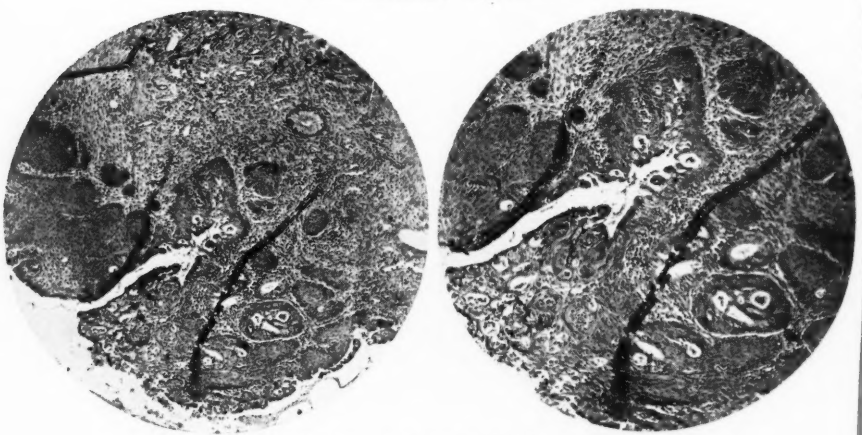


FIG. 14.—*In circle—malignant focus; below—glandular tissue becoming exfoliated.*



FIGS. 15 AND 16.—*Malignant focus under increasing magnifications.*

been able to satisfy myself that a considerable percentage of cervical cancers probably arise during the unsuccessful healing of the chronic types of cervical erosion. As the malignant change arises during the healing process when this is repeatedly frustrated by chronic irritation, there can be little doubt that by applying strong chemical irritants to erosions which are still unhealed after a period of years we copy very exactly the conditions under which cancer has been produced experimentally in animals.

Thus, when an erosion has reached such a stage of unhealed chronicity that atypical squamous overgrowth is likely to be present, local irritants should be avoided and wide excision practised.

THE TREATMENT OF CERVICAL EROSION, WITH SPECIAL REFERENCE TO THE "PRE-CANCEROUS" CERVIX.[1]

BY

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EROSION of the cervix uteri is one of the commonest of gynæcological conditions seen, both in hospital and in general practice. Practically every other patient examined in a gynæcological out-patient department is found to be suffering from this condition in either a mild or a severe form. Sometimes it is but part of a general endocervicitis and endometritis, but in many cases it is the only abnormal condition present.

First I must refer briefly to the so-called "congenital erosion of the cervix," a term which is in a large number of cases a misnomer. In the true congenital erosion there is an overgrowth of the columnar epithelium at the expense of the squamous epithelium covering the cervix around the external os. This gives rise to an absolutely circular velvet patch surrounding the os, which is often seen in the new-born and may persist in adolescence. This patch becomes a ready focus for infection, and may account for the persistence of some cases of vulvo-vaginitis in children.

In a large number of cases, however, the so-called "congenital" erosion is due to a gonococcal infection of the cervix. In this condition the erosion is not

[1] A Paper read at the Bath and Bristol Branch of the British Medical Association, May 26th, 1926.

absolutely circular and often gives rise to small localised granulomata, inflammatory in origin.

Few cases of true congenital erosion require treatment, but if it is associated with leucorrhœa then one or two applications of pure carbolic acid may be made to the cervix. This may necessitate a preliminary incision of the hymen under local anæsthesia, but in the majority of cases the application may be made through a glass tube by means of a piece of wool on a wooden holder.

If the erosion is due to gonorrhœal infection (and this applies to any gonorrhœal cervical infection), the best treatment is local application of flavine or mercurochrome to it, after it has been cleansed of mucous discharge by means of a solution of sodium bicarbonate or weak liquor potassæ. The vagina and fornices are afterwards packed lightly with ribbon gauze soaked in flavine or mercurochrome.

We come now to the treatment of the common erosion of the cervix, which in practically all cases results from infection of a laceration occurring during labour. In these cases the treatment depends on three things, the age of the patient, the extent and kind of erosion, and the co-existence or not of other uterine disease.

In a simple case of erosion, for example that which is limited to the laceration of a recent confinement, and does not spread beyond this over the squamous-lined cervix, astringent douches will in the majority of cases effect a cure. Of these lead acetate, alum or zinc sulphate are the best, and these should not be given hot but nearly cold in order to get the best effect. At the same time attention should be paid to treatment of the general health of the patient, by regulation of the bowels, rest and suitable tonics, especially iron. If

astringent douches fail to effect a cure, then repair of the cervical tear by operation is to be advised; the scar tissue and erosion are excised by a V-shaped incision and the edges of the V sutured together.

The application of strong caustics, especially repeated application, to the cervix, is not only inadvisable, but actually harmful. They cause deep sloughing with consequent formation of cicatricial tissue which leads to trouble in later pregnancies, and may be the starting-point in the formation of carcinoma of the cervix. In support of this statement may be quoted the case of Mrs. W., upon whom I operated in August, 1924.

This patient was an actress, 2-para, aged 35, who had suffered for several years from a vaginal discharge, and had for the six months previous to coming under my care been treated with applications of zinc chloride to the cervix. When I saw her she had an extensive squamous-celled cervical carcinoma, which on removal was seen to be growing from an area of dense cicatricial tissue. In my opinion this carcinoma was started by the application of strong caustic.

If the erosion has extended beyond the laceration, and especially if it is of the papillary type, thorough removal of the eroded area, either by curettage or excision with subsequent suture, is advisable. Even if the patient does subsequently become pregnant the cervix, after excision and suture, dilates quite evenly and does not tend to tear much more readily than the normal cervix.

Attention is particularly directed to a class of case in which the patient is around the menopausal age and complains of a continuous muco-purulent discharge. On examining the cervix it is found to be-covered, or partially so, with an extensive proliferative erosion which bleeds slightly on examination. There is no definite ulceration and no macroscopic sign of carcinoma.

In other areas of the cervix partial healing of the erosion may have taken place, leaving a hard surface studded with ovulæ. I class all these cases as "pre-carcinomatous," that is, cases in which a carcinoma may arise and is indeed very likely to arise. In these circumstances I recommend a total hysterectomy, with conservation of one or both ovaries, depending on their condition. To many this may seem a too drastic and unnecessary course, so I will endeavour to justify it.

It is universally recognised that carcinoma of the cervix arises in the large majority of cases in women who have borne children. In most if not in all these patients there has been a preliminary cervical laceration. Commencing thus, the process continues to the formation of an erosion to which sepsis is added, the result being a chronically infected surface constantly bathed with pus and subject to perpetual irritation, conditions recognised as ideal for the development of carcinoma. Then again, in the healing process the columnar epithelium being replaced and invaded by the squamous epithelium, in the menopausal age 45–50 and after, there seems to be a loss of tissue balance ; the squamous epithelium piles itself up and often breaks through the basement membrane, a carcinoma resulting.

It is impossible to discern with the naked eye the early carcinomatous changes, and even if one takes a section of the erosion one may not hit on the one small area of commencing carcinoma.

As an example of this, we have the case of Mrs. K., whom I first saw in November, 1925. She had at this time a typical pre-carcinomatous cervix. I advised pan-hysterectomy, to which she agreed ; but she did not come in when sent for, and did not report again until six months later, when there was present a carcinoma visible to the naked eye.

As an alternative to pan-hysterectomy, there is amputation of the cervix ; but by this means one does

not remove all the cervical tissue, and a number of growths arise at the level of the internal os. Further, the body of the uterus remains, which in these cases is nearly always in a condition of chronic endometritis and metritis. Finally, at this age, *i.e.* around the menopause, the uterus is a functionless and useless organ.

The operative risk of total hysterectomy is extremely small, and even amputation of the cervix has a small operative risk. I have performed total hysterectomy for this type of case thirty-six times during the last twelve months, in hospital and private practice, without a single death. In my opinion the death rate from carcinoma of the cervix will be enormously lessened by radical operation on these pre-carcinomatous cases. It is better to remove a small number of functionless uteri, which may not develop carcinoma, than to allow a large number to go on to the formation of carcinoma, which can only be removed by an extensive operation with a 40 per cent. mortality.

PLATE X.

RENAL DISEASE.

FIG. 1.

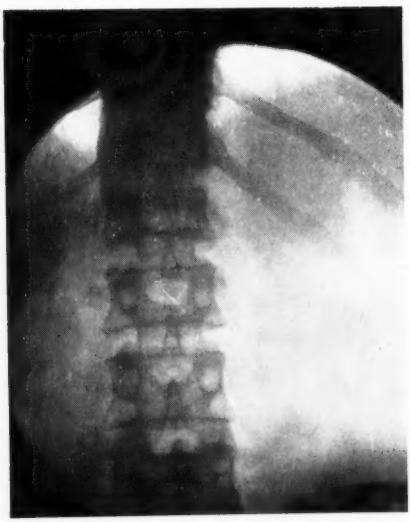

FIG. 2.

THE INVESTIGATION OF SURGICAL CASES OF RENAL DISEASE.[1]

BY

D. G. C. TASKER, B.Sc., M.S., F.R.C.S.,

Assistant Surgeon, Bristol General Hospital.

So much has appeared lately in the medical literature about renal efficiency from a medical aspect that I thought to-day you would be interested in seeing how modern methods of estimation of renal efficiency are applied to surgery.

I have in the wards a patient, a woman of 48, who for five years has had attacks of typical renal colic, and an X-ray (Fig. 1) shows a large calculus in the right kidney.

I propose to carry out before you to-day, in her case, the examination used as a routine for all renal cases, and I will first briefly explain the steps involved.

Investigation of renal cases falls into four steps :—

1. Clinical examination.
2. X-ray examination.
3. Cystoscopy.
4. Operation.

The clinical examination comprises a discussion with the patient of the usual symptoms associated with urinary disease : pain, disturbance of micturition, and the usual clinical examination of the patient abdominally, per rectum, and possibly per urethram, ending with an examination of the urine. Other facts that can be

[1] A postgraduate demonstration.

elicited in the clinical examination of importance in estimating renal efficiency I will mention later.

X-ray examination can rarely be omitted, and there are two main points to which I would draw your attention. *First, the whole urinary tract must be X-rayed.* Three films are required in every case, namely, one of each kidney and one of the pelvis to include the bladder and lower portions of the ureters. Even though you are quite confident that the symptoms are due to a lesion in one kidney, the other kidney and the bladder must also be X-rayed. This X-ray (Fig. 2) will emphasise this point. It shows the left renal area of a woman who had typical attacks of renal colic on the left side only. It is entirely negative. At the same time, as a routine, the right renal area was X-rayed

You will see in this X-ray (Fig. 3) several large and very definite stones. Not a pain nor an ache occurred on the right side, yet removal of the stones from the right side cured the pain on the left side. This is not an isolated case, as each year there are usually two or three examples of this referred renal colic found in the X-ray Department of the General Hospital.

Another reason for X-raying the whole urinary tract is that stones in the lower part of the ureter may give rise to pain solely in the loin and renal area, and *vice versa.* Therefore, once you have decided to have a patient X-rayed, insist on three films being taken in every case.

The second point in the X-ray examination is that the *X-rays must be good ones.* This, theoretically, goes without saying; but a certain amount of time and trouble are required before this is attained, both on the part of the doctor in charge of the case and on the

PLATE XI.

RENAL DISEASE.

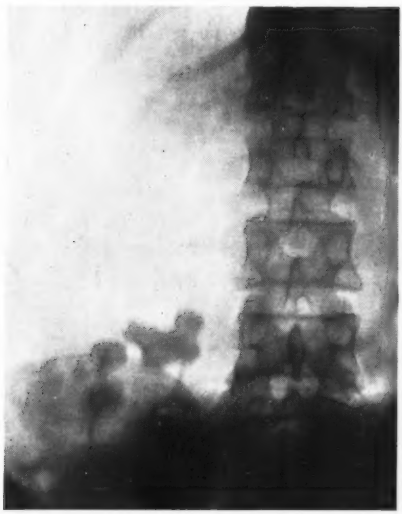

FIG. 3.

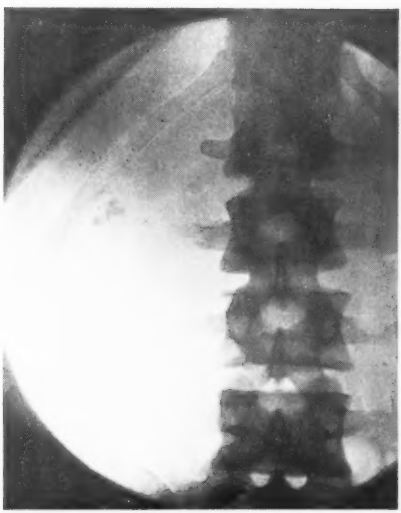

FIG. 4.

radiologist's part. Your part consists in the proper preparation of the patient by giving an aperient the night before, and arranging for an enema a few hours before the examination. The enema can be dispensed with, but the aperient never. A practical point is that an oily aperient such as castor oil should not be given, as this seems to leave an opaque coating to the colon making it show up, thus obscuring the renal areas. The preparation by aperient and enema is necessary to get rid of gas and opaque fæcal material in the colon.

The radiologist's part consists of the correct exposure and development of the films, and it is probable that these details are known better by those of you who take their own X-rays than by me. The criteria of satisfactory renal X-rays are :—

1. The colon should be invisible.
2. The outline of the psoas muscle must be clearly visible.
3. The outline of the kidney itself should be seen. This last point is sometimes impossible to attain in fat patients.

However, even with the most careful X-ray examination wrong diagnosis will be made. Fig. 4 shows a collection of small shadows in the right renal area of a man who had had repeated attacks of apparently typical renal colic. These shadows were visible in each of three sets of X-rays taken. Cystoscopy gave no information, and at length I explored the right kidney and ureter, palpating the interior of the kidney and the pelvis with a finger introduced through an incision in the cortex of the kidney. No sign of any stone was found.

The peritoneum was then opened and the biliary apparatus was explored with a negative result. I stitched the right kidney up, as it seemed somewhat mobile, and I am glad to say that the patient has had

no symptoms of any kind since. An X-ray taken some six months after the operation shows the shadows still there.

Cystoscopy is the next step required in dealing with a renal case. This may seem unnecessary in a patient with a clear shadow showing in the X-ray, but we have to guard against several eventualities that I will detail later.

The cystoscopic examination consists of :—

(1) *Examination of the bladder and ureteric orifices.* This enables cystitis, vesical stone, and papillomata to be excluded. It will also guard one from mistakes in cases having only one kidney and ureter. The ureteric orifices are to the urinary tract what the tongue is to the alimentary canal ; if they are of normal size and not inflamed, it can be taken as certain that there is no gross disease of the kidneys, and *vice versa.*

(2) *Catheterisation of both ureters,* thus enabling a specimen of urine to be withdrawn from both kidneys separately.

(3) *Observation of the rate of excretion of a dye* that has been injected previously into the general circulation.

Thus by cystoscopy we can tell the functional capacity of each kidney separately. It may be that when we come to operate on a kidney in which an X-ray shows a stone, we find that the kidney is hopelessly disorganised ; or (as I have seen happen once) beside a stone being present, there is an entirely unsuspected malignant disease for which nephrectomy is necessary. It then becomes of paramount importance to know whether there is another kidney, and also whether it is sound enough to warrant remōval of the kidney in question.

It is, of course, well recognised that a single kidney only may be present. The figure usually given for this

is that it occurs about once in every five thousand individuals. Fig. 5 may bring this fact home to you. This is a drawing of the bladder of a patient in which only one kidney was present, and you will see that there is an entire absence of a left ureteric orifice.

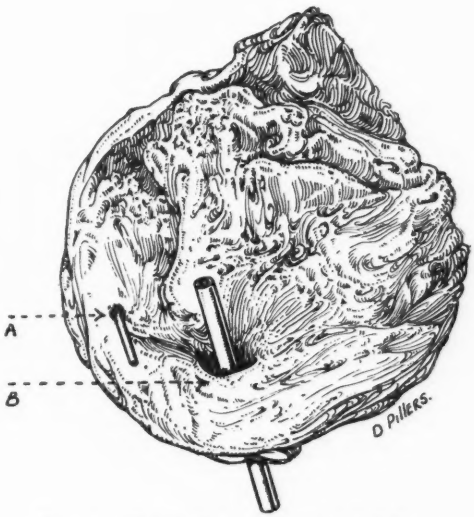

FIG. 5.—*Congenital absence of left kidney.*
Drawing of bladder, showing absence of ureter.
A.—Probe in right ureteric orifice. B.—Larger probe in urethra orifice.
Note absence of left ureteric orifice.

Besides the evidence of the presence or absence of a kidney, catheterisation of the ureters tells us whether the other kidney has sufficient functional capacity to allow of removal of the diseased kidney if required; and it also tells us, by the tests I will describe later, whether the capacity of both kidneys together is sufficient to warrant an operation on one kidney. It is no rare occurrence for a patient to have a stone in one kidney, or some condition demanding an operation on the kidney, and for the other kidney to be almost

out of action from some latent disease. Patients in this state develop a fatal uræmia with startling suddenness after an operation, however trivial, on one kidney.

To prevent operation on patients with latent uræmia, three tests are carried out :—

1. *Urea Concentration Test.* This test, popularised by Maclean, is adapted to the catheterisation of the ureters as follows : Two and a half hours before the time fixed for the cystoscopy a draught containing 15 grammes of urea in 100 c.c. of distilled water is given to the patient and the bladder is emptied. One hour after this the patient passes urine again, and this is saved and labelled " Specimen No. 1." Two hours after the taking of the urea solution the patient passes urine again, and this constitutes " Specimen No. 2." Half an hour after this the patient is taken to the theatre and the cystoscope is passed, either with or without an anæsthetic, and the bladder and ureters are inspected. By the end of the third hour from the giving of the urea solution a catheter should be in each renal pelvis and a specimen, which need not exceed 5 c.c. in amount, is collected from each kidney simultaneously. These constitute " Specimen No. 3 (right) and (left)." The percentage of urea in each of these four specimens is estimated.

This test consists in giving a large dose of urea and estimating the manner in which the kidney is able to deal with it. If the kidneys have a safe margin of functional capacity they will respond to this excess of urea by excreting it rapidly, so that Specimens Nos. 2 and 3 (right) and (left) will all contain over 2 per cent. of urea. If the percentage of urea is less than 2 per cent. we then know that the kidneys are incapable of dealing with any increased strain put upon them, and that they are

very near the threshold of uræmia. Specimen No. 1 is neglected if the result is less than 2 per cent., as it is found that urea in itself is a diuretic and causes an excessive secretion of water which will dilute the percentage of urea in this specimen. This diuresis passes off within an hour, hence the later specimens are unaffected.

By this method of carrying out the urea concentration test (by obtaining the third specimen from each kidney separately) not only can the functional capacity of both kidneys together be estimated but also that of each kidney separately, a most valuable piece of information.

2. *Indigo-Carmine Excretion.* Directly specimens for the preceding test have been obtained, 4 c.c. of a 0·4 per cent. solution of indigo-carmine is injected into a vein in the arm. With a normally acting kidney, within seven minutes and usually at the end of four minutes, puffs of dark blue urine can be seen ejected through each ureteric orifice. If none appears in ten minutes, it is certain that that kidney is of very little functional use. This test will act as a control on the results obtained from the preceding test, and only prolongs the examination by a few minutes.

3. *The estimation of the percentage of urea in the blood* is useful as a control of the capacity of both kidneys together, but it can only be carried out by examination of the blood in a fully-equipped pathological laboratory.

Clinical Examination. These tests may seem somewhat complicated, and it may be a relief to you to know that for the purpose of estimating the total renal capacity none of them are more valuable than the evidence that can be obtained from the clinical examination.

The following points in the history give a good notion of the total functional capacity of the kidneys :—

(1) Headaches.
(2) Vomiting, especially unrelated to meals.
(3) Appetite for meat. Loss of appetite is one of the earliest signs of renal impairment.
(4) Thirst.

On examination note should be taken of :—

(5) The tongue ; a dry furred tongue associated with
(6) Dry skin is an almost certain sign of latent uræmia. Other points to be noted are a raised blood-pressure and signs of cardiac enlargement.

The value of these clinical data is of great use when, as sometimes happens, the various chemical tests do not correspond with each other. When there is any doubt the evidence from the clinical examination should be the determining factor.

Cystoscopic examination of the patient was then carried out, with the following results :—

Examination of the bladder and ureteric orifices was normal.

Specimen No. 1=2·25 per cent. urea.
Specimen No. 2=2·70 per cent. urea.
Specimen No. 3 (right)=2·80 per cent. urea.
Specimen No. 3 (left)=3·00 per cent. urea.

Indigo-carmine was seen to be excreted through both ureteric orifices in less than seven minutes.

A week later the calculus was removed from the right kidney, and after an uneventful convalescence the patient left the hospital free from symptoms sixteen days after the operation.

A CASE OF SEVERE HERPES ZOSTER AND VARICELLA OCCURRING SIMULTANEOUSLY IN AN AGED PATIENT.

BY

R. E. Overton, M.R.C.S., L.R.C.P.

(Corsham, Wilts.)

The patient was a remarkably active old gentleman of 93 years and 6 months. He had enjoyed excellent health all his life, and at the onset of his illness was driving out each day and taking a lively and controlling interest in his affairs. The only physical defect was an ankylosis of his left hip joint and some three inches of shortening in the left leg following fracture of the neck of the femur thirty years ago.

On April 18th, 1926, I was consulted, as Mr. X. had then been complaining for three days of—

(1) Slight sore throat.

(2) Stabbing pains in the right side of the neck and jaw and over the right shoulder. The pain was instantaneous, and seemed to "dart right through his head."

(3) Insomnia owing to the pain—the latter being worse at night.

The patient looked ill. He was fully dressed and unwilling to submit to a proper examination. Such of the skin as could be inspected appeared normal. There was no hyperæsthesia, and at the time of the consultation the patient was quite comfortable and free from pain.

Phenazone gr. x was prescribed, to be repeated every six hours. The patient had a fairly comfortable night.

April 19th, 1926. The following day an extensive rash of herpes zoster was present over the whole area of the third and fourth cervical nerves on the right side. Many of the vesicles contained a dark blood-stained fluid. A great number had been scratched and were bleeding. The vesicular area was surrounded by a small margin of erythema. The temperature was normal, but the pain continued in severity and frequency.

An ointment containing 3 per cent. yellow mercuric oxide was applied on lint over the whole area.

April 20th, 1926. The day after the rash was at its maximum. Large areas had become infected, and there was considerable sloughing of the skin. The region which had been pressed on by the back collar-stud was the worst, and here quite a deep slough was present.

April 21st, 1926. On the third day of the rash the dressing had to be discontinued owing to a mercurial dermatitis. It was replaced by calamine lotion and starch poultices in the area of the beard.

April 22nd, 1926. Lymphatic enlargement in the right axilla was considerable and painful. There was very marked œdema of the right arm and dorsum of the hand.

April 23rd, 1926. The patient's general condition gave rise to some alarm. Pain, lack of sleep and the disturbances necessitated by the dressings had fatigued him considerably. In view of his advanced age and his own inclinations it was considered inadvisable to insist on his taking to his bed.

April 24th, 1926. On the fifth day after the appearance of the herpes the patient developed a

generalised varicella. The vesicles extended over the whole body, most marked on the back and abdomen. (About two hundred vesicles were present altogether.) A few vesicles were present on the face and limbs, and about a dozen on the scalp. This rash followed the course of a perfectly typical chicken-pox, passing through the papular, vesicular and scab stages. In ten days from the commencement of the varicella all evidence of it had disappeared.

May 4th, 1926. By this time the herpetic area had almost completely healed. In this same area, however, severe attacks of shooting pains were still a constant feature; itching and the sensation of "small animals crawling about" were causing a great deal of discomfort. The enlargement of the axillary lymphatics subsided with the sepsis. Sleep could only be obtained artificially, gr. xx each of chloral and bromide being given alternately at night with gr. v of barbitone.

The general disturbance of the chicken-pox appeared to be much greater than that of the herpes, so that on May 5th the patient had become so feeble that he was unable to leave his bed. He then for the first time became completely helpless and despondent. The herpetic lesions had quite healed, but in that area the loss of sensation was almost complete; in only very few of the least involved areas was the patient able to feel sharp stabs with a pin. Discrimination between hot and cold was entirely absent.

May 15th, 1926. After a period of ten days, during which the patient was perfectly helpless and bedridden, he began slowly to improve.

June 17th, 1926. He now drives out again every day, and appears to be as well both physically and mentally as he was before the onset of the disease.

Mr. X. tells me—and his memory is extremely

good—that he has never had either of these diseases before.

It is over thirty years since the first account was published of cases in which herpes zoster was associated with varicella. Reviews of the subject have been published from time to time, and of late interest has been revived by reports of cases in this country, in France and elsewhere. A perusal of these records (as abstracted in recent volumes of the *Medical Annual*) shows that there are three kinds of reported association ; chicken-pox may arise after contact with herpes in another person, herpes may similarly arise after contact with chicken-pox, or the eruption of varicella may follow that of herpes after an interval of a few days, in the same individual.

It appears, also, that three explanations of this association have been advanced. First, it is suggested that the eruption described as varicella is really that of herpes zoster generalisatus. To the present instance this hypothesis does not seem applicable. The two eruptions each ran their course typically and separately. That of herpes was strictly limited to the original area, and so were the nervous phenomena which lingered after its subsidence. The varicellar rash, on the other hand, was scattered after its normal fashion over the trunk, and its component elements passed through the stages customary in varicella.

Second, it is sought to explain the association away as a mere coincidence. Both for and against this hypothesis a great many arguments have been marshalled, and a single case can scarcely move the balance of opinion in either direction. During the period when this patient's case was under observation about a dozen examples of chicken-pox, on the one hand and a similar number of cases of herpes, on the

other, were noted in the same district. Was this a coincidence, or was it a further piece of evidence in support of the third hypothesis ?

This seeks to prove an identity of causation for the two diseases ; no easy task, since we are so far without clear knowledge of the virus of either. Much has been made, on both sides, of arguments based on the immunity said to be conferred by one disease against the other. In this instance the patient was immune against neither. The fact that he had escaped immunisation until an advanced age might serve to explain the severity of the infection when at last it did attack him.

Reviews of Books.

Brain and Heart. By GIULIO FANO. Translated by HELEN INGLEBY with a Foreword by Prof. E. H. STARLING. Pp. xv., 142. Humphrey Milford, Oxford University Press. 1926. Price 8s. 6d. net.—Mr. Milford is to be congratulated on publishing these lectures of the great Italian physiologist, since, as Professor Starling says in his Foreword, they represent an epitome of the life work of a very great master, and Professor Fano is to be congratulated that this brief survey of his work has been presented to English readers by such an admirable translation, which preserves the freshness and charm of the original and at the same time presents the subject-matter so easily and clearly. The first two lectures are on "the so-called living matter." After reviewing the recent advances in physics and chemistry in explaining many processes which we observe in living matter, he scouts the idea that these bring us any nearer the understanding of life. Living matter is merely the form taken by the life force, and as such is relatively unimportant. Almost, but perhaps not quite, he persuadeth us to believe that Bergson has said the last word in philosophy. In the next two lectures he describes experiments which show that the whole hierarchical arrangement of the nervous system subserves a series of superimposed inhibitions, till finally the discriminative will of man is made possible by inhibitions of inhibitions in lower levels of function. In the last two lectures, on excitability and automatism, he describes his experiments on the excised hearts of animals and embryos, which show that as we extend the scale in the history of the race the individual automatism gives place to excitability in inverse proportion, and how in the case of the heart the high automatism and low excitability of the auricular end and the high excitability and low automatism of the ventricular end explain most of the modern problems of cardiology.

Surgery of Childhood. By JOHN FRASER, M.C., M.D., Ch.M., F.R.C.S. (Eng.). 2 vols. Pp. viii., 604; iii., 609–1152. London: Arnold & Co. 1926.—The surgery of childhood differs so materially from that of adults that the appearance

of these volumes by Professor Fraser will be welcomed by all those whose work lies to any extent in the treatment of children. Taken as a whole, the construction of the work leaves little to be desired. Some of the rarer deformities might well have been relegated to text books of orthopædics, and some portions (notably the surgery of the spleen) could have been amplified with advantage. Naturally a good deal of the book deals with orthopædic surgery, which forms so large a part of the work of any children's hospital, but the author has selected his material with care, and summarised judiciously. The chapters dealing with surgical tuberculosis are excellent, and the article on the making of celluloid splints could hardly be improved upon. In Volume I. the description of the various methods for the treatment of burns is particularly valuable. The book is thoroughly up to date and includes a good deal of recent work. Printing, illustrations and index are good, and there are unusually few typographical errors. Any surgeon would find it quite a sound investment.

Tuberculous Disease of the Hip Joint. By George Perkins, F.R.C.S., Assistant Surgeon to the Royal National Orthopædic Hospital. Pp. 118, figures 32. Humphrey Milford, Oxford University Press. Price 6s.—This, the first "Robert Jones" prize monograph, is a clear and simple account of hip disease. The diagnosis of only the early stages is considered and a number of most excellent X-ray pictures greatly help the text. A follow-up of 50 cases with description of late results as related to the type of disease and method of treatment is the most valuable feature of the book.

Radiotherapy in Relation to General Medicine. By F. Hernaman-Johnson, M.D. Pp. viii., 211. Humphrey Milford, Oxford University Press. 1926. Price 5s. net.—This little book, essentially non-technical, is alive with sane and suggestive thought upon the subject of Radiant Energy and its uses and limitations in the art of Therapeutics. The title adequately expresses its scope, and it should do much to counteract extreme and uninformed views about this rather difficult subject, and at the same time stimulate a real interest in the great and still relatively unexplored possibilities of Radiotherapy in relation to general medicine. Rarely has one come across a book of this type which can be so heartily recommended, both to the general practitioner or surgeon and to the specialist.

When one reflects that matter is now considered as a form of energy, that life in all its forms is a manifestation of energy, and that the cause of its evolution has been largely determined by Radiant Energy—life has been bathed in various forms of Radiant Energy since its birth—it becomes obvious that in artificially-produced radiations we have a most potent addition to our therapeutic armamentarium, the intelligent study of which becomes almost a duty, when one considers the present state of medical science. The author, after reviewing in a most interesting manner the physics and biological effects of Radiation, discusses at some length the general nature of disease and what we can hope for in the action of remedies—this chapter might have been condensed somewhat—and proceeds to bring Radiation-Therapy into line with other forms of treatment. The latter half of the book deals more specifically with his experiences and suggestions in dealing with the Cancer problem, and the treatment of various infective and endocrine disturbances, and he ends with a strong plea for an intelligent combined attack on disease, using such therapeutic agents as we now have at our command, not as a blunderbuss, but in proper and rational combination, and directed by specialists, who are also " general practitioners " in their medical outlook, working in co-operation.

The Medical Annual. 44th Year. Pp. 616. Bristol: John Wright & Sons Ltd. 1926. Price 20s. net.—The great value of the *Annual*, now in its forty-fourth year, is so universally recognised that it needs no recommendation here. The present issue is an excellent one, but many who esteem its invaluable accounts of recent improvements in treatment, diagnosis and prevention of disease seem to be ignorant of its " special guide " sections—its lists of recent and new books, classified, and giving the prices and publishers, those of institutions, homes and sanatoria, of medical and scientific societies and periodicals, of Life Assurance Offices, of manufacturers of new appliances, of many official boards (by the way, we miss the Board of Control), such as the personnel of the General Medical Council and the Ministry of Health. Now these are of the greatest use to the busy practitioner and add much to the value of the book. Then, too, there are indexes, published separately every ten years, helpful for those who have access to the back volumes. In this way anyone working up a subject thoroughly can find references to and abstracts of most of the important papers on his subject in

English journals during recent years. In no other way can he so quickly get an outline of what has been done and its results. The aid thus given by the *Annual* to scientific study is unique and of national importance. We are anxious to draw attention to these features of the book, though the very interesting details in the present volume of recent advances in medicine and surgery might well take up our space.

Favourite Prescriptions. By Espine Ward, M.D. (Belfast). Pp. 96. London: J. & A. Churchill. 1926. Price 5s.—This is a small book which contains a large number of prescriptions which should be useful to the newly-qualified practitioner, but a distinct danger in the hands of the more ignorant general public. Its value is greatly diminished in that these prescriptions are arranged under the headings of definite diseases, and not under the headings of the principal drugs prescribed. The following are examples of the danger attending the course adopted by the author: There is only one prescription for such diseases as Pneumonia and Bright's Disease in its many forms. Under the head of Epilepsy we find three prescriptions containing bromides, but no reference is made to the value of luminal in these cases. It would appear to be rather dangerous to suggest arsenic as the proper treatment for eczema in all its protean forms, and still more dangerous to prescribe sulphonal in small repeated doses for mania. In spite of the above criticisms, there are many prescriptions which should be useful and suggestive to the busy practitioner. The hints for the treatment of poisoning at the beginning of the book are handy, concise and valuable.

Editorial Note.

A Country Hospital for Bristol Cripples.

For the past five or six years the inadequacy of Bristol's provision for the treatment of crippling disease, especially in children, has been troubling the minds of many people. Good work has been and is still done by the Orthopædic Hospital, the Children's Hospital, and by the two big general hospitals; and to this must be added the care for patients with surgical tuberculosis provided by the Municipal Council, who have had the great disadvantage of possessing no premises of their own for the purpose. It is, in fact, this lack of means for treating the patients for whose welfare they are by law responsible that has brought the City Health Committee to formulate proposals for the development of an orthopædic hospital at Frenchay Park, an estate that was bought by the city on favourable terms when it came into the market.

Now, side by side and always in touch with this municipal movement, there has developed a voluntary movement, embodied in the Crippled Children's Society, of which Miss F. M. Townsend is President. This Society has for some years done excellent work on behalf of the Crippled Children of Bristol, including among these children with heart disease and other affections that are indeed "crippling," though not always so described. It has recently become united with the Orthopædic Hospital in Redland, and the two

bodies have decided to build a country school-hospital as soon as they have funds enough. They made proposals for union with the municipal hospital, which were examined by the Ministry of Health, but as the Ministry reported in favour of a plan by which the voluntary body would provide a kind of convalescent home for the patients from the city's Orthopædic Hospital and for other patients, the hopes of union have been somewhat dashed. The Voluntary Committee, also, thinks that some site better than the Frenchay one might be found, and indeed has been looking carefully into the possibilities of a country site with a protected southerly aspect.

There can be no doubt that the medical profession will support a policy of union. Their wish for united effort in the treatment of crippling disease in childhood has found expression again and again, and Professor Hey Groves has exerted himself greatly to bring it about. Neither can there be any two opinions about the question of a site. It ought to be the best that the neighbourhood offers, and it must be large enough to allow of the addition of new blocks. The big voluntary hospitals of the city can hardly hope to extend their in-patient provision on their present sites, and much has already been said of the possibility of a gradual migration to the outskirts of the city. It would be a thousand pities if anything were to ruin the city's chance of uniting forces in the near future, and we earnestly hope that the long view will prevail.

The Medical Library of the University of Bristol,

WITH WHICH IS INCORPORATED

The Library of the Bristol Medico-Chirurgical Society.

The following donations have been received since the publication of the List in June, 1926.

	October, 1926.
W. P. Eagleton, M.D. (1)	1 volume.
Professor E. Fawcett (2)	1 ,,
Professor E. W. Hey Groves (3)	4 volumes.
The Medical Officer of Health of Bristol (4)..	1 volume.
The Registrar (5)	3 volumes.
Sir Humphry Rolleston (6)	1 volume.
The United Fruit Company (7)	2 volumes.

Unbound periodicals have been received from Professor Hey Groves.

THE ONE HUNDRED AND SEVENTEENTH LIST OF BOOKS.

The figures in round brackets refer to the figures after the names of the donors. The books to which no such figures are attached have either been bought from the Library Fund or received through the *Journal*.

Bassi, A.	*Opere*		1925
Bland-Sutton, Sir J., and Giles, A. E.	*Diseases of Women* ..	8th Ed.	1926
Browne, F. J.	*Advice to Expectant Mother on the Care of her Health*		1926
Cathcart, G. C.	*Tod's Diseases of the Ear*	2nd Ed.	1926
Cochrane, W. A. ..	*Orthopædic Surgery*		1926
Cope, Z.	*Treatment of the Acute Abdomen*		1926
Eagleton, W. P. ..	*Cavernous Sinus Thrombophlebitis*	(1)	1926
Fairbairn, J. S.	*Obstetrics*		1926
Gibson, A. G.	*The Heart*		1926
Graham, G.	*Pathology and Treatment of Diabetes Mellitus*	2nd Ed.	1926

Library

Howard, R., and Perry, A.	*The House-Surgeon's Vade-Mecum*	2nd Ed.		1926
Ibbotson, W.	*Surgical Operations*	2nd Ed.		1926
Jordan, A. C.	*Chronic Intestinal Stasis, a Radiological Study*	2nd Ed.		1926
Knaggs, R. L.	*Inflammatory and Toxic Diseases of Bone*			1926
de Lint, J. G.	*Atlas of the History of Medicine. I. Anatomy*			1926
MacKenzie, Sir James	*Principles of Diagnosis and Treatment in Heart Affections*	3rd Ed.		1926
Mandl, F.	*Chirurgie der sportunfaelle*		(3)	1925
Pannett, C. A.	*Surgery of Gastro-duodenal Ulceration*			1926
Pinch, A. E. H.	*Manual of Technique in Radium Therapy*		(2)	1926
Porritt, N.	*The Abdomen in Labour*			1926
Riddell, J. R.	*Medical Electricity and Radiology*			1926
Rolleston, Sir Humphry	*Jaundice, Diseases of Liver and Biliary Tract*		(6)	1926
Scott, R. J. E.	*Gould's Medical Dictionary*	8th Ed.		1926
Snowman, J.	*Manual of Emergencies*	2nd Ed.	(3)	1926
Thomson, A., and Miles, A.	*Manual of Surgery.* 2 Vols.	2nd Ed.	(3)	1926
Thomson, F. G., and Gordon, R. G.	*Chronic Rheumatic Diseases*			1926
Thomson, Sir St. Clair	*Diseases of the Throat*	3rd Ed.		1926
Tomson, W. B.	*Notes and Suggestions for the Finding of Employment for the Tuberculous*			1926
Vallery-Radot, P.	*Oeuvres de Pasteur.* Vol IV.			1926
Watson, J. K.	*A Handbook for Nurses*	7th Ed.		1926
Williams, L.	*Obesity*			1926

TRANSACTIONS, REPORTS, JOURNALS, ETC.

Annual Report of the Medical Officer of Health, Bristol, 1925	(4)	1926
British Journal of Surgery, Vol. XIV., No. 53 (July)		1926
Cancer Review, Vol. I., No. 1		1926
Collected Papers of the Mayo Clinic, Vol. XVII., 1925		1926
Dental Board of the United Kingdom: General Anæsthesia		1926
Guy's Hospital Reports, Vol. LXXVI., No. 3 (July)		1926
Minutes of General Medical Council, Vols. LIII. [1916], LIV. [1917], LV. [1918]	(5)	
Progressive Medicine (March) and (June)		1926
St. Bartholomew's Hospital Reports, Vol. LIX.		1926
Surgical Clinics of North America (June)		1926
United Fruit Company, Medical Department: Thirteenth and Fourteenth Annual Reports, 1924 and 1925	(7)	—

Local Medical Notes.

EXAMINATION RESULTS.

University of Bristol.—Students of the University have recently passed the following examinations :—

BRISTOL, L.D.S., R.C.S.—*First Professional—Part I.:* R. A. Phillips ; *Part II.:* R. A. Phillips, R. G. Boodle, C. Haskins, W. Woolley ; *Part III.:* A. F. N. Shapland. *Final—Part I.:* J. F. V. Sellin ; *Part II.:* A. W. M. Anderson, A. G. Batten, V. M. S. Jones, R. Y. Simpson, H. B. Smith.

L.S.A.—*Primary Examination (in Anatomy):* G. Smith. (*In Physiology*) *:* L. P. Gregory, G. Smith.

F.R.C.S.—*Primary :* R. A. S. Cory, A. C. Fisher, K. H. Pridie. *Final :* F. Langford.

M.R.C.S., L.R.C.P.—G. L. Feneley.

UNIVERSITY OF LONDON, M.B., B.S.—*Second Examination—Part II.:* P. Dalzell, L. E. Vine, K. H. Pridie. *Third Examination :* W. H. Royal.